HRM 730
Introduction to Research Methods for Randomized Controlled Trials

COURSE OBJECTIVE

This course will introduce students to the main elements of clinical trial design, execution and analysis. At the end of this course, students should have a firm grasp of clinical trial methodology at a level that would allow them to prepare successfully grant applications.

COURSE FORMAT

- 11 units, one per week
- Each unit will consist of a large group session from 1:00 to 2:15pm, followed by a tutorial from 2:30 to 4:00pm
- Large group sessions will be directed by a faculty member who will introduce the main issues, distilled "wisdom", and challenges associated with the unit.
- Each tutorial group will have from 8 to 10 students.
- Tutors will make every effort to participate in all of the weekly large group sessions, and particularly those following which they will be tutoring.
- The tutorial will focus on questions students wish to raise concerning their attempt to deal with the same issues in their protocols.
- Each student will prepare a written research protocol for a clinical trial on a topic of their own choosing. Protocols will be presented by the student at the end of the course and reviewed by a fellow student and faculty member.

COURSE EVALUATION

25% = Contribution to tutorials

Weekly participation marks are based on your involvement during each session and are assessed weekly by the tutor.

Please note that the course coordinator does not have access to the evaluations. Summary statistics are provided by the HRM Administrative Assistant and cannot be linked to any specific person.

50% = Production and presentation of a Research Protocol

25% = Written and verbal review of a fellow student's protocol

DESCRIPTION OF UNITS

1. INTRODUCTION

- Explain course format, assignments, evaluation
- Review units and common themes: bias avoidance, feasibility, ethics
- A brief history of clinical trials
- The importance of the study questions

2. STUDY DESIGNS

- The following study designs will be discussed:
  - Parallel
  - Cross-over
  - Factorial
  - Cluster
  - Expertise-based
  - Non-inferiority
  - Equivalency

3. THE POPULATION

- Inclusion criteria (definition of the population of interest)
- Exclusion criteria (unsuitable individuals with the disease)
- Mechanistic/explanatory versus Practical/Pragmatic trials
- Subgroup analysis

4. RANDOMIZATION

- Why do we randomize, what does it accomplish?
- Is stratification (by center, patient characteristics) needed?
- How to produce a randomization schedule (random number tables, blocking within strata)
- How to deliver the randomization schedule (central call-in, envelopes, packaged meds)
- Randomization ratios (1:1, 2:1, etc.)
- Minimization
- Adaptive allocation

5. GENERAL MEASUREMENT ISSUES

- Who should measure the outcome?
- When should it be measured?
- How should it be measured?
- Selecting the “best” outcome measure
- Quantitative measures into event outcomes
- Avoiding measurement bias

- Adjudication committees
- Reliability and validity

6. INTERVENTION

- Specify Your Precise Experimental and Comparison Regimens
- Identify the Source and "Packaging" of Your Regimens
- Set Up a System for Distributing and Maintaining Supplies of Your Regimens
- Set Up a System for Emergency Code-Breaking (When Patients and/or Clinicians are Blind)
- Set Up a System for Maintaining Blindness (When Patients and/or Clinicians are Blind)
- Decide What to do About Monitoring (and, if Necessary, Improving) Patient Compliance
- Design Follow-up Procedures
- Set Up a System for Avoiding (and Documenting) Contamination and Cointervention
- Set Up a System for Maintaining Protocol Adherence by Your Collaborators

7. OUTCOME EVENTS

- Detailed consideration of issues association with outcome events

8. THE ANALYSIS PLAN, PART I (Scientific Decisions)

- What analysis strategy best matches the research question
- Primary and secondary analyses
- Supporting mechanistic/explanatory analyses
- Efficacy and intention to treat analyses
- Deciding whether to adjust for baseline risk factors
- Anticipating missing data and problem cases
- Interim analysis
- Adjustment for multiple outcomes

9. THE ANALYSIS PLAN, PART II (Basic and Advanced Statistical Methods)

- Baseline description and comparisons
- Differences between: quantitative, event, and time to event outcomes
- Hypothesis testing
- Estimation and confidence intervals
- Displaying results (tables and graphs)
- Sample size and power calculations
- Confounding, stratification and adjustment

10. TRIAL ORGANIZATION / ADMINISTRATION / FINANCE

- Executive, steering and monitoring committees
- Committee composition and roles
- Budget preparation
- Centre funding mechanisms
- Patient recruitment strategies
- Patient recruitment logs
- Centre feedback: status reports and newsletters

11. TRIAL MANAGEMENT AND QUALITY CONTROL

- CRF design issues
- Data collection strategies
- CRF/data quality control
- Plans for data management
- Database integrity checks
- Estimating data flow and manpower requirements
- Site visits
- Data audits

12. PROTOCOL PRESENTATIONS

IMPORTANT INFORMATION

If you choose to do a "design" thesis, it cannot be on the same topic as your HRM730 protocol.

REFERENCE MATERIALS

The following text is required:

Haynes, RB, Sackett, DL, Guyatt, GH, and Tugwell, P. Clinical Epidemiology: How to do clinical practice research. Philadelphia: Lippincott, Williams & Wilkins. 2006

Available at the Health Sciences Bookstore

Other helpful references:

From the Health Sciences Library

Title: Management of data in clinical trials
Author: McFadden, Eleanor
Publication Date: 2007

Title: Fundamentals of clinical trials
Author: Friedman, Lawrence M
Publication Date: 1998

Title: Design and analysis of clinical trials: concept and methodologies
Author: Chow, Shein-Chung
Publication Date: 2004
Call Number: QV 771 .C552d 2004

Title: Guide to clinical trials
Author: Spilker, Bert
Publication Date: 1991
Call Number: QV 771 .S756gb 1991

Title: Wiley Encyclopedia of Clinical Trials
Info: The online site for definitive reference on all facets of clinical trials.
On-campus Access: http://mrw.interscience.wiley.com/emrw/9780471462422/home/
Off-campus Access:

1. login to Libaccess (with your McMaster ID and PW)
https://libraryssl.lib.mcmaster.ca/libaccess/login.php?url=http://library.mcmaster.ca/loggedip.htm

2. put this URL into the same web browser you used to get to Libaccess
http://mrw.interscience.wiley.com/emrw/9780471462422/home/

From the Health Sciences Bookstore (Mediashop)

Title:	Randomised controlled trials
Author:	Jadad, Alejandro
Publisher:	BMJ Books
Publication Date:	2007
Price:	$42.99

Title:	Fundamentals of clinical trials
Author:	Friedman, Lawrence M
Publication Date:	1998
Price:	$90.95